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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,352	06/29/2007	Francis X. Smith	3009094 US01	1290

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EXAMINER	
GUPTA, ANISH	

ART UNIT	PAPER NUMBER
1654	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/593,352	SMITH ET AL.	
	Examiner	Art Unit	
	ANISH GUPTA	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 August 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7, 9-14, 16-19* is/are rejected.

7)☒ Claim(s) *8,15 and 20* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendment filed 8/17/10 is acknowledged. Claims 2 was amended and claims 8-20 were added. Claims 1-20 are pending in this application.

Maintained Rejections

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

1. Claims 1-7 remain rejected and new claims 9-14, and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over De Bruiju et al. (WO0007634) in view of Schwab et al. (Animicrob. Agents Chemother.).

The claims are drawn to ophthalmic solution comprising a peptide of SEQ ID NO 1, NO 2 or NO. 3.

De Bruiju et al. teaches numerous contact lens solutions which contain an antimicrobial and are active against different microbes including *P. aeruginosa*. The reference specifically disclose the use of Benzyldimethyl [2-[2-(p-1,1,3,3-tetramethylbutylphenoxy)ethoxy]ethyl] ammonium chloride as the antimicrobial agent. The reference also discloses the addition of various agent to enhance compatibility with the eye. For example, the reference disclose the use of buffers such as citrate, borate, HEPPS, HEPES and the like to avoid irritation and sting to the eye (see page 7, lines 14-22). The reference also teaches that sequestering agents such as gluconate or tartarate can be utilized as preservatives, disinfectants or cleaning solutions (see page 8, lines 5-11). The reference states that decanedoic acid improves ocular comfort of contact lens solutions. The reference disclose the addition of glycerin .2% and .2% decanedioic acid (see example 4 and 5). The reference also states that glycerin improves the kill of *P. aeruginosa* (see page 12, example 3). The difference between the prior art and the instant application is that the reference does not teach the use of any of the specific peptides claimed.

However, Schwab et al. teaches conducts antimicrobial activity experiments against *P. aeruginosa* using designed antimicrobial peptides (DAPs) in different buffers (see abstract). The DAPS specifically utilized include D2A21, D4E1 and D5C (see page 1436). It should be noted that D2A21 and D4E1 correspond to SEQ ID NO 2 and SEQ ID NO 1 of the claimed invention. The reference discloses results which indicate that both D4E1 and D2A21 demonstrate the highest antimicrobial activity against *P. aeruginosa* (see page 1436, figure 2). While the conclusions are for patients with cystic fibrosis, the reference concludes that DAPs are attractive as therapeutic agents because their activities do not appear to be diminished over a wide range of osmolarities. Therefore,

it would have been obvious to one of ordinary sill in the art to use D2A21 or D4E1 with the ophthalmic solutions of De Bruiju et al. because both D2A21 or D4E1 had more antimicrobial activity against *P. aeruginosa*. There would have been a reasonable expectation of success because both D2A21 and D4E1 are designed antimicrobial peptides that are active against *P. aeruginosa*.

Response to Arguments

Applicants argue that the instant claims recite that the sodium chloride solution is not greater than .2 weight percent, which is not taught in the prior art. Applicants also state that the references are in widely divergent field and should not be combined. Applicants assert that Schawb et al. is directed to treatment of lung infections due to cystic fibrosis and does not teach ophthalmic solutions. Applicants state that this treatment method is not the same endeavor as the ophthalmic solutions.

Applicants arguments have been fully considered but have not been found persuasive.

With respect to the concentration of the chloride, the MPEP states "Generally, differences in concentration or temperature will not support the patentability of subject matter encompassed by the prior art unless there is evidence indicating such concentration or temperature is critical. "[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955) (Claimed process which was performed at a temperature between 40°C and 80°C and an acid concentration between 25% and 70% was held to be prima facie obvious over a reference process which differed from the claims only in that the reference process was performed at a temperature of 100°C and an acid concentration of 10%.); see also Peterson, 315 F.3d at 1330, 65 USPQ2d at 1382 ("The normal desire of scientists or artisans to

improve upon what is already generally known provides the motivation to determine where in a disclosed set of percentage ranges is the optimum combination of percentages.""

In the instant case, the prior art teaches "To avoid stinging or irritation it is important that the solution possess a tonicity and pH within the physiological range, e.g., 200-350 mOsmole for tonicity and 6.5-8.5 for pH. To this end, various buffering and osmotic agents are often added. The simplest osmotic agent is sodium chloride since this is a major solute in human tears." The instant specification states "[t]he tonicity of the solutions typically adjusted to approximately 240-310 millimoles per kilogram solution (mOsm/kg) to render the solution compatible with ocular tissue and with hydrophilic contact lenses." (see page 7). The specification then defines the concentration of the sodium chloride between .01 to .2 weight percent. Since the prior art teach the same mOsmole for tonicity, it would have been obvious to optimize the chloride concentration to arrive at 200-350 mOsmole for tonicity. Thus, the reference does teach a concentration of NaCl of less than .2 weight percent.

With respect to Schawb, unlike Applicants contentions, the prior art is not in a different filed of endeavor. The primary reference teaches the addition of antimicrobial agents to be active against different microbes including *P. aeruginosa*. .The purpose of using the peptides in the contact solution is for the same purpose. The reference of Schwab et al.discloses results which indicate that both D4E1 and D2A21 demonstrate the highest antimicrobial activity against *P. aeruginosa* (see page 1436, figure 2). Thus, while the conclusions are for patients with cystic fibrosis, the reference concludes that DAPs are attractive as therapeutic agents because their activities do not appear to be diminished over a wide range of osmolarities. The field of endeavor for both reference is therapeutic formulations that are active against *P. aeruginosa*. Therefore, it would have been obvious to one of ordinary sill in the art to use D2A21 or D4E1 with the ophthalmic solutions of De Bruiju et al.

because both D2A21 or D4E1 had more antimicrobial activity against *P. aeruginosa*. There would have been a reasonable expectation of success because both D2A21 and D4E1 are designed antimicrobial peptides that are active against *P. aeruginosa*.

Rejection is maintained.

2. Claims 1-3 and 6 remain rejected and new claims 9-14, and 16-19 are under 35 U.S.C. 103(a) as being unpatentable over Sousa et al. in view of Schwab et al. (Animicrob. Agents Chemother.).

The claims are drawn to ophthalmic solution comprising a peptide of SEQ ID NO 1, NO 2 or NO. 3.

Sousa et al. teach ophthalmic formulations that contain a synthetic cecropin peptide D5C. The reference specifically teaches three different commercially available contact lens cleaning solutions to which 100 μg/mL was added (see material and methods on page 115). The solutions utilized were "Renu Multi-Purpose Solution," containing boric acid, edentate disodium, poloxamine, sodium borate, sodium chloride, and polyaminoporpyl biguanide .000005% as a preservative; "Complete All-In-One Solution" containing sodium chloride, polyhexamethylene biguanide, tromethamine, Tyloxapol, and edetate disodium; and "Opti-Free" which contains citrate buffer and sodium chloride, edetate disodium .05% and polyquaternium-1 .0001% (see page 115). Note that the three solutions utilize a buffer recited in claim 3 and the Renu Multi-Purpose Solution contains a poloxamine, which is a polyoxyethylene surfactant. The reference teaches that the three solutions, by themselves, were effective against *P. aeruginosa*. However, the addition of the cecropin peptide augmented their antimicrobial activity in the presence of the contact lens (see abstract). More specifically, the reference states that 100 μg/mL of D5C added to Renu Solution and the Complete solution, both of which contain the biguanide, enhanced antibacterial activity against *P.*

aeruginosa (See page 117). The difference between the prior art and the instant application is that the reference does not teach the use of any of the specific peptides claimed.

However, Schwab et al. teaches conducts antimicrobial activity experiments against *P. aeruginosa* using designed antimicrobial peptides (DAPs) in different buffers (see abstract). The DAPS specifically utilized include D2A21, D4E1 and D5C (see page 1436). It should be noted that D2A21 and D4E1 correspond to SEQ ID NO 2 and SEQ ID NO 1 of the claimed invention. The reference discloses results which indicate that both D4E1 and D2A21 demonstrate the highest antimicrobial activity against *P. aeruginosa* (see page 1436, figure 2). While the conclusions are for patients with cystic fibrosis, the reference concludes that DAPs are attractive as therapeutic agents because their activities do not appear to be diminished over a wide range of osmolarities. Therefore, it would have been obvious to one of ordinary sill in the art to use D2A21 or D4E1 with the Renu and Complete ophthalmic solutions of Sousa et al. because both D2A21 or D4E1 had more antimicrobial activity against *P. aeruginosa*. There would have been a reasonable expectation of success because both D2A21 and D4E1 are designed antimicrobial peptides that are active against *P. aeruginosa* similar to D5C.

3. Claims 1-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sousa et al. in view of Schwab et al. (Animicrob. Agents Chemother.) in further view of De Bruiju et al.

The claims are drawn to ophthalmic solution comprising a peptide of SEQ ID NO 1, NO 2 or NO. 3.

The references of Sousa et al. in view of Schwab et al. have been discussed supra and their motivation for combination has been discussed supra. The difference between the prior art and the

instant application is that the reference does not teach ophthalmic formulations as claimed, with the specific buffer, preservative, wetting agents etc...

De Bruiju et al. teaches numerous contact lens solutions which contain an antimicrobial and are active against different microbes including *P. aeruginosa*. The reference specifically disclose the use of Benzyldimethyl [2-[2-(p-1,1,3,3-tetramethylbutylphenoxy)ethoxy]ethyl] ammonium chloride as the antimicrobial agent. The reference also discloses the addition of various agent to enhance compatibility with the eye. For example, the reference disclose the use of buffers such as citrate, borate, HEPPS, HEPES and the like to avoid irritation and sting to the eye (see page 7, lines 14-22). The reference also teaches that sequestering agents such as gluconate or tartarate can be utilized as preservatives, disinfectants or cleaning solutions (see page 8, lines 5-11). The reference states that decanedoic acid improves ocular comfort of contact lens solutions. The reference disclose the addition of glycerin .2% and .2% decanedioic acid (see example 4 and 5). The reference also states that glycerin improves the kill of *P. aeruginosa* (see page 12, example 3). It would have been obvious to use an ophthalmic formulation as taught in De Bruju because it achieves a formulation that is compatible with the eye. The reference provides motivation to use gluconate or tartarate to be used as preservatives, disinfectants or cleaning solutions, specific buffers to avoid irritation and sting to the eye, glycerin to improves the kill of *P. aeruginosa* and decanedoic acid to improve ocular comfort of contact lens solutions.

Response to Arguments

For both rejection Applicants raise similar arguments and these have been discussed below.

Applicants argue that the instant claims recite that the sodium chloride solution is not greater than .2 weight percent, which is not taught in the prior art. Applicants also state that the references are in widely divergent field and should not be combined. Applicants assert that Schawb et al. is

directed to treatment of lung infections due to cystic fibrosis and does not teach ophthalmic solutions. Applicants state that this treatment method is not the same endeavor as the ophthalmic solutions.

Applicant's arguments have been fully considered but have not been found persuasive.

All of the three formulations taught in the prior art are sold in the market as nonirritating to the eye. It is known in the art that if the concentration of the buffer is too high, it will cause irritation to the eye. For example, De Bruiju et al. teaches "[t]o avoid stinging or irritation it is important that the solution possess a tonicity and pH within the physiological range, e.g., 200-350 mOsmole for tonicity and 6.5-8.5 for pH. To this end, various buffering and osmotic agents are often added. The simplest osmotic agent is sodium chloride since this is a major solute in human tears." Similarly, Applicants specification states "[t]he tonicity of the solution is typically adjusted to approximately 240-310 milliosmoles per kilogram solution (mOsm/kg) to render the solution compatible with ocular tissue and with hydrophilic contact lenses." (see page 7). The specification then defines the concentration of the sodium chloride between .01 to .2 weight percent. Note that the prior art tonicity is similar to what is taught in the specification. Given the teaching of the prior art, that one must maintain a tonicity and pH within the physiological range, e.g., 200-350 mOsmole for tonicity and 6.5-8.5 for pH to avoid stinging and irritation, the concentration of the chloride must be below the claimed range.

The MPEP states "[w]here the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. In re Best, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the

burden of showing that they are not." In re Spada, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Therefore, the prima facie case can be rebutted by evidence showing that the prior art products do not necessarily possess the characteristics of the claimed product. In re Best, 562 F.2d at 1255, 195 USPQ at 433." In the instant case, there is ample reason to believe that the concentration of the sodium chloride is the same as the claimed invention. One can make this conclusion because one must maintain a tonicity and pH within the physiological range, e.g., 200-350 mOsmole for tonicity and 6.5-8.5 for pH to avoid stinging and irritation. The concentration of sodium chloride to achieve this tonicity will be less than the claimed range. Applicants have not provided any evidence that the prior art product, those available in the market, contain a concentration that is higher than the claimed range. If Applicants believe that the concentrations are indeed different, then Applicants are requested to provide evidence that this is the case.

With respect to the different field of endeavor, unlike Applicants contentions, the prior art is not in a different filed of endeavor. The primary reference teaches the addition of antimicrobial agents to be active against different microbes including *P. aeruginosa.* The purpose of using the peptides in the contact solution is for the same purpose. The reference of Schwab et al.discloses results which indicate that both D4E1 and D2A21 demonstrate the highest antimicrobial activity against *P. aeruginosa* (see page 1436, figure 2). Furthermore, and more importantly, the primary reference teaches the use of a cecropin peptide D5C in the ophthalmic solutions. This same peptide is also taught in Schwab as being effective against *P. aeruginosa.* Given the teachings of both Sousa et al. and Schwab et al. with respect to D5C, one would have concluded that cecropin peptides can be used in both ophthalmic solutions and treatment of cystic fibrosis. Accordingly, the field of endeavor for both references is therapeutic formulations that are active against *P. aeruginosa.* Therefore, it would have been obvious to one of ordinary sill in the art to use D2A21 or D4E1 with

the ophthalmic solutions of De Bruiju et al. because both D2A21 or D4E1 had more antimicrobial activity against *P. aeruginosa*. There would have been a reasonable expectation of success because both D2A21 and D4E1 are designed antimicrobial peptides that are active against *P. aeruginosa*.

Rejection is maintained.

4. Claims 8, 15 and 20 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

5. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

6. Any inquiry concerning this communication or earlier communications from the examiner should be directed to ANISH GUPTA whose telephone number is (571)272-0965. The examiner can normally be reached on 5/4/9.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Tsang Cecilia can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/
Primary Examiner, Art Unit 1654